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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,583	08/17/2001	John A. Browse	4630-58963	6370

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/857,583	BROWSE ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14,16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,14,16 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-11, 14, 16 and 18 are currently pending in this application.

Election/Restrictions

Applicant's election of Group I, claims 1-11, 14, 16, and 18 in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is drawn to an isolated nucleic acid comprising a sequence as shown in SEQ

ID NO:2. However, a perusal of sequence listing shows that SEQ ID NO:2 is an amino acid sequence and not a nucleic acid sequence. Therefore, it is not clear to the Examiner whether applicants are claiming a nucleic acid sequence or an amino acid sequence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9, 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a desaturase enzyme comprising the amino acid sequence SEQ ID NO:4, encoded by the polynucleotide with SEQ ID NO:1-3 does not reasonably provide enablement for any such enzyme that is at least 60% identical to SEQ ID NO:4 or any desaturase that is encoded by a nucleotide sequence that hybridizes under low stringency hybridization conditions to SEQID NO:3 or fragments thereof or 10 consecutive nucleotides of SEQ ID NO:3 under any hybridization condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 9, 18 are so broad as to encompass any desaturase from any source comprising at least 60% identical to SEQ ID NO:4 or any desaturase that is encoded by a nucleotide sequence that hybridizes under low stringency hybridization conditions to SEQID NO:3 or fragments thereof or 10 consecutive nucleotides of SEQ ID NO:3 under any hybridization condition. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of desaturases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single desaturase. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides as claimed. The specification is limited to teaching the use of SEQ ID NO: 4 and those polypeptides encoded by SEQ ID NO:1-3 as a desaturase but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the

claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any desaturase with 60% identity to the enzymes of SEQ ID NOS:4 or any desaturase encoded by a nucleotide sequence that hybridizes under low stringency hybridization conditions to SEQID NO:3 or fragments thereof or 10 consecutive nucleotides of SEQ ID NO:3 under any hybridization condition because the specification does not establish: (A) regions of the protein structure which may be modified without affecting desaturase activity; (B) the general tolerance of desaturases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including desaturases with an enormous number of amino acid

modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of desaturases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 2-8, 10-11, 14, 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA with SEQ ID NO:1, 2 or 3 encoding a desaturase enzyme, does not reasonably provide enablement for any such DNA encoding a desaturase enzyme having 60% amino acid sequence identity with SEQ ID NO:4, or any DNA which is 60% identical to SEQ ID NO:1 (no specific function, see claim 6) or any such DNA encoding a desaturase enzyme which hybridizes under low stringency conditions with the polynucleotide SEQ ID NO:3 or fragments thereof, or any such polynucleotide encoding a desaturase enzyme which hybridizes to at least 10 contiguous nucleotides of SEQ ID NO:3 under any hybridization conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 2-8, 10-11, 14, 16 are so broad as to encompass any DNA encoding a desaturase enzyme having 60% amino acid sequence identity with SEQ ID NO:4, or any DNA which is 60% identical to SEQ ID NO:1 or any DNA encoding a desaturase enzyme, which hybridizes under low stringency conditions with the polynucleotide SEQ ID NO:3 or fragments thereof, or any such polynucleotide encoding a desaturase enzyme which hybridizes to at least 10 contiguous nucleotides of SEQ ID NO:3 under any hybridization conditions, and vectors and host cells comprising such DNAs. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above polynucleotides for processes such as recombinant protein preparation, as hybridization probes, for identification of mRNA etc. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and since only nucleic acids with very high percent homology can be used as a probe for either identifying mRNA or for screening a cDNA library, changing the nucleotide sequences as proposed by the applicants and/or addition of substantial amount of additional nucleotide sequence unrelated to the nucleic acid sequence of SEQ ID NO:1 through 3 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of nucleotide sequences that could hybridize to several unrelated mRNAs instead of hybridizing specifically to mRNA of interest and similarly may hybridize to cDNAs totally unrelated to the cDNA of interest while screening a cDNA library.

However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single desaturase enzyme with SEQ ID NO:4. Furthermore, while the specification teaches that SEQ ID NO:1 encodes a desaturase, claim 6 is silent regarding the function of polynucleotide that is 60% identical to SEQ ID NO:1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence that can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding a protein having desaturase activity because the specification does not establish: (A) regions of the DNA sequence which may be modified without effecting the above mentioned activity/utility; (B) the general tolerance of desaturase encoding DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in a polynucleotide encoding a desaturase with an expectation of obtaining the desired biological function and utility; (E)specific function of polynucleotide that are 60% identical with SEQ ID NO:1 and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any DNA encoding a desaturase enzyme having 60% amino acid sequence identity with SEQ ID NO:4, or any such DNA which is 60% identical to SEQ ID NO:1 or any such DNA which hybridizes under low stringency conditions with the polynucleotide SEQ ID NO:3 or fragments thereof, or any such polynucleotide which hybridizes to at least 10 contiguous nucleotides of SEQ ID NO:3 under any hybridization conditions. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 6 is directed to a transformed cell transformed with a genus of DNA molecules having 60% identity with SEQ ID NO:1 and transformed with the polynucleotide encoding the desaturase of claim 1. While applicants have described the structure and function of the polynucleotide encoding desaturase of claim 1, they have failed to fully describe the polynucleotide that has 60% sequence identity to SEQ ID NO:1 that is also used to transform the cell.

The specification does not contain any disclosure of the function of all DNA sequences that are 60% identical to SEQ ID NO:1. The genus of DNAs that comprise these above DNA

molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

MANJUNATH RAO
PATENT EXAMINER

Manjunath N. Rao
August 27, 2003